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CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.
11TH FLOOR, SEVEN PENN CENTER
1635 MARKET STREET
PHILADELPHIA, PA 19103-2212

| EXAMINER | |
|---|---|
| HA, JULIE | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1654 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 01/23/2009 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@crbcp.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/500,093 | KHALAF ET AL. | |
| | Examiner | Art Unit | |
| | JULIE HA | 1654 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *65-74 and 95-122* is/are pending in the application.

4a) Of the above claim(s) *67-69,71-74,95-100, 103 and 109-122* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65,66,70 and 104-108* is/are rejected.

7)☒ Claim(s) *70, 101-102, 105* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/6/2005 and 9/25/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Responses to Election/Restriction filed on July 03, 2008 and October 21, 2008 are acknowledged. Claims 1-64 and 75-94 have been cancelled and new claims 95-122 have been added. Claims 65-74 and 95-122 are pending in this application.

***Restriction***

1. Applicant's election with traverse of Group 3 (claims 65-74, 78-82 and 94) in the reply filed on July 3, 2008 and October 21, 2008 are acknowledged.

2. The traversal is on the ground(s) that the restriction requirement does not conform to the PCT unity of invention rules in that lack of unity was not found in the PCT application and the instant application is a national stage entry of the PCT application. This is not found persuasive because while the national and regional Offices may not make further requirements beyond those of the Treaty and Regulations in respect of matters of form and contents, they are not bound by the Treaty to follow the results of any international search or examination which has been performed when the application is examined during the national or regional phase (see International Search and Preliminary Examination Guidelines page 15 paragraph 1.12). There is no core structure shared by all of the compounds. The only core structure shared by all compounds is that they all have an NH group. Therefore, for the reasons presented in the previous office action, the restriction requirement is still deemed proper and is therefore made FINAL.

3. The elected invention N-[3-(dimethylamino)propyl]2-({[4-({[4-(formylamino)-1-methyl-1—pyrrol-2-yl]carbonyl}amino)-1-methyl-1H-pyrrol-2-yl]carbonyl}amino)-isopropyl-1,3-thiazole-4-carboxamide appears to be free of prior art. The search was extended to the linking claims and prior art was found on compound of formula I. Claims 109-122 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 67-69, 71-74, 95-100 and 103 are withdrawn from further consideration, as being drawn to nonelected species compound found in the prior art. Claims 65-66, 70, 101-102, 104-108 are examined on the merits in this office action.

***Objection***

4. Claims 101-102 and 105 are objected for reciting nonelected inventions in the claims. Applicant is advised to cancel all claims drawn to nonelected inventions.

5. Claim 70 is objected to for the following minor informality: claim 70 recites, "...the structural fragment of formulae Ia, Ib, Ic, Id, Ie and If are as defined in any one of claims 16 to 20..." Claims 1-64 have been cancelled.

***Rejection***

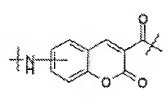
***35 U.S.C. 112, 2nd***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 65-66, 70, 103-108 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claim 65 recites, "...E represents $-E^1$-$Het^4$-, $-E^{2a}$, $-(CH_2)_{0-3}N(H)C(O)-E^{2b}$-$C(O)N(H)(CH_2)_3$- or a structural fragment of the formula  , wherein $E^3$ represent..." and "...each individual Q independently represent a structural fragment of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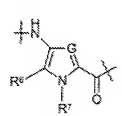
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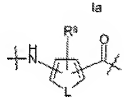
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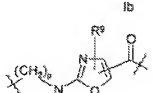
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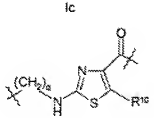
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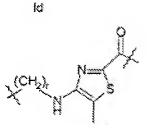
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formula Ia, Ib, Ic, Id, Ie or If ..." It is unclear what structural fragments of these formula the fragments encompass. Because claims 66, 70, and 104-108 depend from indefinite claim 65 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

***35 U.S.C. 112, 1st***

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 65-66, 70, 104-108 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the

conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a compound of formulae I and II wherein there are different variables for both formulas I and II. The generic statements a compound of formulae I and II do not provide ample written description for the compounds since the claims do not describe a single structural feature. The only common core shared by the compound of the formulae is that they all have an NH. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

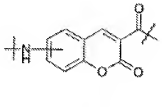
As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claims 65 and 70 are broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that can form peptide or amide bonds, and make up the class of proteins and compounds having the formulae I or II. Further, the only constituent that is required by compounds of formulae I and II is an NH molecule. Therefore, the compound can be any molecule having an NH molecule. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples

in the specification. As described above, the only common core structure shared by all of the compounds is that they all have an NH molecule. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules, and other synthetic peptide or peptide-like molecule that can form peptide bonds, and function as proteins or oligopeptides.

The specification discloses Netropsin, 12/41, 13/20, Distamycin A, 13/51 and 34 different compounds having NH molecule that is shared by all other compounds. The specification discloses that the term "aryl" when used herein, includes C6-10 aryl groups such as phenyl, naphthyl and the like. When substituted, aryl groups are preferably substituted by between one and three substituents (see paragraph [0032] of instant specification US 2007/0117760 A1). The specification discloses that the term "aromatic or part-aromatic C13-14 tricyclic carbocyclyl", when used herein includes fluorenyl, antracenyl, 9,10-dihydroanthracenyl, phenanthrenyl, 9,10-dihydrophenanthrenyl and the like (see paragraph [0033] of instant specification as described above). The specification discloses that the term "halo" includes fluoro, chloro, bromo and iodo. Het ($Het^1$ to $Het^4$) groups may be fully saturated, partly unsaturated, wholly aromatic, partly aromatic and/or bicyclic in character and paragraph [0035] describes examples of $Het^1$ to $Het^4$. The compounds of formulae I to VI have different variables that can be vast

number of components that could lead to innumerable numbers of compounds. The only component that is shared by all of the formulae is the NH molecule.

The working example 1 describes making of the compound N-[5-({[3-Diemthylamino)propyl]amino}carbonyl)-1-methyl-1H-pyrrol-3-yl]amino}carbonyl]-1-isopropyl-1-H-pyrrol-3-yl]-4-[(3,3-dimethylbutanoyl)amino]-1-methyl-1H-pyrrole-2-carboxamide. All of the working examples (1-36) describe making of the 34 different compounds. Description of 34 compounds (in name only, no structures provided) and 5 different structural compounds is not sufficient to encompass numerous other compounds having the NH molecule that belong to the same genus. For example, there are varying lengths, varying amino acid compositions, varying components and variables and numerous distinct qualities that make up the genus. For example, the specification discloses that $R^1$ represents $Het^1$, $R^{1a}C(O)$- or D-A-N(H)-$[Q]_n$-C(O)-E-C(O)- wherein $R^{1a}$m A represents different components, D represents different components, R2a, R2b, R4, E, R1, E2a, E2b, Het1 to Het4, R3a, R3b, R5, Q and other variables represent different components. Furthermore, E and Q represent structural fragment of



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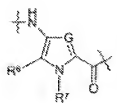

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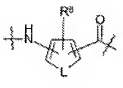

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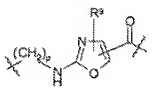

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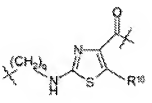

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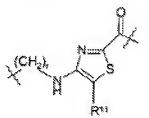

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the formulas  and .

Since these are fragments of these structures, they can be any fragment, leading to innumerable structural compounds. Again, the different possibilities depend on the different variables and components, leading to innumerable compounds. The claims do not describe a single structural feature, except that they all share the NH molecule. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention. Therefore, there is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed. The MPEP §2163 recites, "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional

characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus...when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. **For inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus."**

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

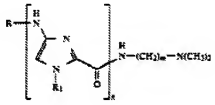
***35 U.S.C. 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

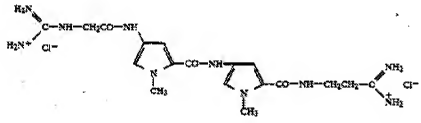
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 65-66, 70 and 104-108 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee Moses NF (US Patent No. 5,273,991, filed with IDS).

13. Lee teaches a oligopeptide derivatives that are conjugated to DNA alkylating agents having the formula  wherein m is 0 to 4; n is 2 to 4, each R1 is the same or different and is hydrogen or C1-C4 alkyl; and R is a DNA alkylating moiety. Furthermore, the reference teaches pharmaceutical compositions (see abstract). The reference teaches that R is $-CO(CH_2)_pR_3$; $-CO(CH_2)_pCH(R_3)_2$; $-CO(CH_2)_pC(R_3)_3$; $-(CH_2)_pAN(R_4)_2$; or $-(CO)(CH_2)_pAN(R_4)_2$, meeting the limitation of compound of formula I (see column 3). The instant claim 65 recites that $R^1$is $R^{1a}C(O)$- wherein $R^{1a}$ is $C_{1-4}$ alkyl, $C_{1-12}$ alkyl (optionally substituted with halo). The reference teaches that pharmaceutical compositions contain the compounds of the invention in combination with pharmaceutically acceptable carrier, meeting the limitation of claim 108. The reference teaches the compound of instant claims, thus the compound would inherently have the same properties and characteristics as the claimed invention. This meets the limitation of claims 104-107. Therefore, the reference anticipates claims 65-66, 70 and 104-108.

14. Claims 65-66, 70 and 104-107 are rejected under 35 U.S.C. 102(b) as being anticipated by Lown et al (US patent No. 4,912,199, filed with IDS).

15. Lown et al teach oligopeptide anticancer and antiviral agents having the formula



wherein $R^1$ is D-A-N(H)-$[Q]_n$-C(O)-E-C(O) and D is $-C(=NR^{2c})N(R^{2d})R^{2e}$, meeting the limitation of claims 65-66 and 70. The reference teaches the compound of instant claims, thus the compound would inherently have the same properties and characteristics as the claimed invention. This meets the limitation of claims 104-107. Therefore, the reference anticipates claims 65-66, 70 and 104-107.

***Conclusion***

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. H./
Examiner, Art Unit 1654

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654